INTERNATIONAL INSTITUTE OF SYNTHETIC RUBBER PRODUCERS, INC.

January 26, 2004

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Ms. Anna Lee Sabella
Report on Carcinogens Group
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Re: National Toxicology Program's Public Meeting to Discuss the Review Process and the Listing/Delisting Criteria Used for the Report on Carcinogens

Dear Ms Sabella:

The International Institute of Synthetic Rubber Producers, Inc. (IISRP) is pleased to respond to the National Toxicology Program's (NTP's) request for comments on the Review Process and the Listing/Delisting Criteria Used for the Report on Carcinogens (FR Vol 68, No 232, Pages 67692--67696). We have attended several public hearings on substances are used by my member companies so we have sincere interest in the RoC process. As noted in our comments we believe that if the process is more open to experts that it will significantly enhanced.

We also fully support comments submitted to you by the American Chemistry Council (ACC), under separate cover. In particular, pursuant to ACC's recommendations, we urge NTP to consider strengthening the scientific quality and public participation processes in the development of RoC actions, and clarifying its listing/delisting criteria used for the RoC.

Sincerely,
James L. McGraw
[Redacted]

Managing Director & CEO
International Institute of Synthetic Rubbers Producers, Inc.

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# COMMENTS ON NTP'S REPORT ON CARCINOGENS PROGRAM

January 27-28, 2004
**Bethesda, MD**

*Presented by International Institute of Synthetic Rubber Producers, Inc*
*Houston, Texas*
*James L. McGraw*
*Managing Director & CEO*

## INTRODUCTION

The NTP has an important role in this country, and it is in the best interests of the regulatory & regulated communities, the public, and future generations that the organization be considered objective and beyond reproach as it carries out its functions in establishing chemical classifications pertaining to cancer causation. Lessons taken from the events of September 2001 include the daunting observation that there are clear & *bona fide* hazards & risks that threaten our lives, families, and the existence of societies and cultures. And it became the highest priority that these be addressed in an appropriate manner. There is a corollary to this – many factors are flagged as hazardous to our citizens, but for which the support is negligible. There is no room in this society for claiming risks for which the evidence is not conclusive.

There are two areas to be addressed in my comments, and these focus upon "science" and "scientists". We in this room all know that an objective & informed classification of chemicals as carcinogens results only from utilization of disciplines applied in a manner considered unequivocally "scientific". In order for science to be properly executed, it is imperative that it be conducted according to scientific principles by individuals who are not only adequately trained in the applicable disciplines, but who think/probe/question & operate in accordance with the scientific method. This has not been the history of deliberations involving chemicals listed in the Reports on Carcinogens.

## SCIENCE

Now that the claim has been made, the support for this is as follows:

- **Selective use of data** - The current process does not practice inclusion of all information relevant to chemical classifications. Repeatedly, commentators have made the point that NTP support documents ignore submitted information, and it is axiomatic that when chemical classifications are developed, the outcome can be substantially influenced by the scope of data made available (Slide 1). *The lack of information makes valid conclusions impossible.*

- **Semantic deception-1** – Over the last few years, NTP has employed the practice of reporting tumor incidences for "benign or malignant tumors". Why is this so problematic? First of all, the higher the malignancy rates parallel increases in doses, the greater the evidence for the chemical's carcinogenic activity. A reviewer needs to know – is the chemical exposure associated with malignancies? (sl. 2). *Do these data support "clear evidence"? No way!* Secondly, the stated basis for combining tumor rates has been "benign" tumors are known to progress to malignancies. However, NTP reports typically provide zero supporting evidence that this situation exists. If this progression is likely to occur, this progression should be seen in the aged rodents at the end of these bioassays. The impact of this combining practice is that there are chemicals being classified a possessing "clear evidence of carcinogenicity" based solely upon the presence of benign tumors.

  Why might this approach be used? One criterion for "reasonably anticipated to be human carcinogen" is when test information "indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors (in animal studies)." This practice impacts the RoC classifications in that "clear evidence" in animals contributes significantly to assigning a RoC classification. Slide 3 shows the outcome that has erroneously supported "clear evidence". Slide 4 shows the football analogy.

- **Semantic deception-2** - Another example is NTP's recent escalation of assigning a "known human carcinogen" designation to chemicals that are simply not known to be a carcinogenic to humans, but rather have a combination of animal, genetic, or mechanistic data that may be highly suggestive or characteristic of human carcinogens. It would be preferred to avoid needing to address the meaning of the word "known" but this onerous practice demands attention. A few synonyms of "known" are "recognized", "proven", "identified", "acknowledged", & "established", and seemingly, this should be a non-contentious issue. In the 10$^{th}$ RoC, there are 49 substances/classes in the "KHC" category, many of which were entered based on information other than human cancer. It does not pass the "man-on-the-street" test for the meaning of "known". At best, this is shoddy science & logic; at worst, it is deceitful to the public, and mighty bad grammar (sl. 5).

- **Non-responsiveness to comments** – This is the issue that most members of the public find objectionable about the RoC process. Experts on chemicals under review spend significant time preparing what is hoped to be considered constructive and new perspectives to be applied to support documents and discussion, but typically what is encountered is a polite "Thank you" and silence. You wonder "Am I wrong?", "What do they know that I don't?", "They are scientists – did they not understand?"

NTP personnel & supporters indicate there is no obligation to respond (as do regulatory agencies), as it would be too time consuming. It also is a practice that ensures minimal discussion and debate, and this, of course, presents the antithesis of true scientific deliberations (sl. 6).

## SCIENTIFIC EXPERTISE

The RoC process is extremely restrictive in terms of inclusion of *bona fide* expertise. I am referring to the token opportunities presented for input by industry scientists, many whom have spent a significant portion of their careers overseeing toxicology & environmental testing, risk assessments, product stewardship, and regulatory matters on specific chemicals. Most of these individuals are highly qualified, and often become the world's expert on a particular product. The NTP's process of limiting the input & opinions of these experts subjects it to the criticism of practicing exclusionary practices. An objective assessment shows that of all the personnel involved in the RoC process (NTP, other federal personnel, NTP-chosen "experts", the public), the group with the greatest chemical-specific expertise has the least opportunity input (sl. 7). *Read points.*

Combined with this topic is the lurking: *do these industry folks have a bias?* The answer is: I do, and I'll state it. I believe that every chemical should be objectively classified on the preponderance of carcinogenicity evidence. The decision-making should be devoid of concerns of risks, avoid taking a precautionary approach, and present the outcome in an unambiguous manner. Naturally, it is incumbent that any industry that makes, sells, transports, uses a product should ensure that exposures are controlled so as to minimize risks to all flora and fauna, but that is a totally separate function. I also have inclination to do my homework, and to be well versed for those products for which I have responsibilities. I am willing to give my opinions on toxicity issues concerning these products, and expect that I can be wrong or uninformed on some of these issues. But I will be anxious to be enlightened when I err, and I would like to believe others who have an interest in that topic would respond the same *(sl. 8)*.

Without getting into the inherent biases of others involved in the RoC process, and I do mean all others, lets shift to a question to be asked when a party does display a bias – so what?? If the BSC for example is composed of individuals who are competent to be members, then they should be more than able to weed out misleading data and information. Scientific members of the group should be in a questioning mode, and if the majority is not capable of this task, why should they be considered experts, and later to be in a position to vote upon the cancer classification of any chemical? (sl. 9). *Isn't it probable good science committees are not impacted by "bias"?*

The Boards of Scientific Counselors (BSC) have been lauded as representing a diversity of disciplines & organizations. This is true, but it is often asked – what relevant contributions can be made by those who are not trained as epidemiology, cancer mechanisms, or toxicology with expertise in experimental carcinogenesis? Typically, each BSC member is to focus & report on 2 or 3 chemicals, and be sufficiently familiar with the other 6-10 chemicals to be able to vote on its carcinogenicity. Even with an applicable background, the members' have an impossible task of adequately understanding the data for nominated chemicals to serve in a capacity of voting on the classification of carcinogenic agents. Are they doing the best they can? Sure, within the structure of the current process. Is the process producing objective and valid results? No. But honestly, the consequences of over-stating a classification are considered by those in the process to be negligible. No one will go to jail, there is no tangible accountability, and there will be no professional discrediting for being wrong.

Finally, there are a few other indications that there is a basis for suggesting a *modus operandi* existing other than science *(slide 10)*. In this slide, there is a small sampling of quotations heard at past BSC meetings, and it is quite obvious that the members are in a mode other than "is this chemical capable of causing cancer?". "Risks", "safety", "worry", "the children" are terms used in chemical exposure & regulatory matters, but are not pertinent when deciding evidence for chemical carcinogenic potentials.

## CONCLUDING COMMENTS

1. NTP needs to define how it is to function in its RoC role. With its title "National Toxicology Program", it is presumed to have a charter to operate according to toxicological principles, maintaining that toxicology itself is a scientific discipline. Perhaps realities of contemporary American culture & government preclude this agency from performing in such a manner. However, unless its stated goals and the actual process for determining chemical classifications are consistent, NTP will continue to be subjected to questions regarding its mission and credibility.
2. In order to move towards optimizing this position, the RoC process would be well served to incorporate greater involvement by experts on a case-by-case basis. Science is best served when there are open discussions amongst interested and informed parties early in the review process. The current practice of soliciting comments in the final stages of review is not constructive, and leads to the current adversarial climate. *Slide 12* is a proposed scheme on how to design a process with the greatest chances of expert input along with the necessary iterations to achieve best outcomes. The public deserves the best application of scientific expertise available plus assurances that future RoCs will provide information that is technically sound and accurately stated.

## Selective Use of Data

- Who won the game???

| | |
|---|---|
| Washington Redskins | 20 |
| Carolina Panthers | |

## "Clear Evidence?" -1a

| Test Group | Malignant Tumors |
|---|---|
| **Control** | **1** |
| **Low Dose** | **2** |
| **Mid Dose** | **1** |
| **High Dose** | **1** |

## "Clear Evidence?"-1b

| Test Group | Benign Tumors | Malignant Tumors | Combined Tumors |
|---|---|---|---|
| **Control** | **2** | **1** | **3** |
| **Low Dose** | **4** | **2** | **6** |
| **Mid Dose** | **7** | **1** | **8** |
| **High Dose** | **10** | **1** | **11** |

## Semantic Deception-1

- Who won the game???

| | |
|---|---|
| Washington Redskins | 20 |
| Carolina Panthers | 10 (or 30) |

## Semantic Deception-2

- Who won the game???
  - The Washington Redskins ran for 250 yards, passed for 500 yards, intercepted 4 passes, and had 6 sacks of the quarterback.
- Do you really know??

## Non-Responsiveness to Comments

- "Hey, I think Washington won the game!

Response -

"

*silence*

"

## PRODUCERS' EXPERTISE

- Unparalled experience and first-hand knowledge not otherwise available
- Industry sponsors most tox & mechanistic research on products
- Knowledge of manufacturing processes and personnel health effects

## "Restrict the Experts"

- "Hey, I believe Washington won the game!

Response -

- "Sorry Mr. Joe Theismann, we don't need your opinion on this"

## "Concern with Bias"

- "Hey, I believe Carolina won the game" said the hotdog vendor.

Response -

- "The scoreboard says Washington won, & the scorekeeper, crowd & announcers think so, but here we have a biased hotdog guy from Charlotte! Oh my, what do we do now? "

## Significant Regulatory/ Political Tone by BSC

- "NTP is not a regulatory body"
- Saccharin. "..and epid study wasn't an *assurance of safety*".
- "..not convinced we know mechanism in rodents, and that it's sufficiently different from humans that we don't need to *worry*."
- "I'm *worried* that exposure will increase if we delist"
- "We can rule our particular risks but *not risks below the limit of detection*."

## FACTORS FOR IMPROVING SCIENTIFIC ASSESSMENTS

- Enhancement of process to optimize interactions and inputs by expert stakeholders early in report development
- Stricter attention to language and the meaning of words
- Elucidation of RoC guidelines, and ensure process consistent with scientific principles

## Proposed Classification Process